Eph Signaling Controls Mitotic Spindle Orientation and Cell proliferation in Neuroepithelial Cells

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A tight regulation of mitotic spindle orientation is crucial during development and adult tissue homeostasis. It determines cell fate specification and tissue architecture in the context of asymmetric and symmetric cell division, respectively. Two major mechanisms, autonomous and non-autonomous, have been implicated in positioning the spindle during cell division. However, while the intrinsic factors that control spindle orientation have been extensively studied over the past decades, our knowledge about the extrinsic signals that modulate this process is much more limited. Here, we uncover a novel function of the Ephrin-Eph intercellular signaling in controlling mitotic spindle alignment in *Drosophila* optic lobe neuroepithelial cells, through aPKC activity-dependent myosin II regulation. Core components of the mitotic spindle orientation machinery mislocalize in dividing *Eph* neuroepithelial cells and show spindle alignment defects in these cells when they are downregulated. Additionally, Eph loss leads to a Rho signaling-dependent activation of the PI3K/Akt1 pathway and a consequent increase of cell proliferation within this neuroepithelium. Hence, Eph signaling is a novel extrinsic mechanism that regulates both spindle orientation and cell proliferation in the *Drosophila* optic lobe neuroepithelium. Similar mechanisms could operate in other *Drosophila* and vertebrate epithelia.